Label Retaining Cells (LRCs) with Myoepithelial Characteristic from the Proximal Acinar Region Define Stem Cells in the Sweat Gland.

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Public Summary:
In this study we were looking for infrequently dividing and label-retaining cells (LRCs), which allowed us to precisely localize and isolate new skin stem cells with slow-cycling and myoepithelial characteristics restricted to the proximal acinar part of sweat glands (SGs) with basal layer localization. In addition, these cells were not present in the SGs ductal distal region. We identified several Bone Morphogenetic Protein (BMP) pathway genes by transcriptional profiling, confirmed the functional requirement of BMP in SGs formation and demonstrated that SG LRCs possess multipotency and stem cells characteristic in vivo with potential to trans-differentiate into the epidermis during wound healing. In addition, our data also suggests plasticity of sweat glands cells to regenerate both sweat glands and hair follicle in vivo. Collectively, our data emphasize SGs are an alternative source of cells for wound healing with potential translational applications due to their ability to regenerate different skin components such as epidermis, sweat glands and hair follicles

Scientific Abstract:
Slow cycling is a common feature shared among several stem cells (SCs) identified in adult tissues including hair follicle and cornea. Recently, existence of unipotent SCs in basal and lumenal layers of sweat gland (SG) has been described and label retaining cells (LRCs) have also been localized in SGs; however, whether these LRCs possess SCs characteristic has not been investigated further. Here, we used a H2BGFP LRCs system for in vivo detection of infrequently dividing cells. This system allowed us to specifically localize and isolate SCs with label-retention and myoepithelial characteristics restricted to the SG proximal acinar region. Using an alternative genetic approach, we demonstrated that SG LRCs expressed keratin 15 (K15) in the acinar region and lineage tracing determined that K15 labeled cells contributed long term to the SG structure but not to epidermal homeostasis. Surprisingly, wound healing experiments did not activate proximal acinar SG cells to participate in epidermal healing. Instead, predominantly non-LRCs in the SG duct actively divided, whereas the majority of SG LRCs remained quiescent. However, when we further challenged the system under more favorable isolated wound healing conditions, we were able to trigger normally quiescent acinar LRCs to trans-differentiate into the epidermis and adopt its long term fate. In addition, dissociated SG cells were able to regenerate SGs and, surprisingly, hair follicles demonstrating their in vivo plasticity. By determining the gene expression profile of isolated SG LRCs and non-LRCs in vivo, we identified several Bone Morphogenetic Protein (BMP) pathway genes to be up-regulated and confirmed a functional requirement for BMP receptor 1A (BMPR1A)-mediated signaling in SG formation. Our data highlight the existence of SG stem cells (SGSCs) and their primary importance in SG homeostasis. It also emphasizes SGSCs as an alternative source of cells in wound healing and their plasticity for regenerating different skin appendages.